

That which is claimed is:

1. An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor, or an isoform or peptide portion thereof (SMRT co-repressor), or an isolated polynucleotide complementary thereto.

2. The polynucleotide of claim 1, which modulates transcriptional potential of a member of the nuclear receptor superfamily (nuclear receptor).

3. The polynucleotide of claim 2, wherein the SMRT co-repressor comprises a repression domain having

- a) less than about 83% identity with a Sin3A interaction domain of N-CoR set forth as amino acids 255 to 312 of SEQ ID NO: 11;
- b) less than about 57% identity with repression domain 1 of N-CoR set forth as amino acids 1 to 312 of SEQ ID NO: 11;
- c) less than about 66% identity with a SANT domain of N-CoR set forth as amino acids 312 to 668 of SEQ ID NO: 11; or
- d) less than about 30% identity with repression domain 2 of N-CoR set forth as amino acids 736 to 1031 of SEQ ID NO: 11, and polynucleotides that hybridize thereto under stringent conditions.

4. The polynucleotide of claim 1, wherein the SMRT co-repressor is a human SMRT co-repressor having an amino acid sequence as set forth in SEQ ID NO: 5 or conservative variations thereof.

5. A polynucleotide which hybridizes under stringent conditions with a polynucleotide according to claim 2.

SUB
A21

Sub C1

SUB
A22

5

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Sub C1

SUB
A23

6. A polynucleotide that has at least 80% sequence identity with a polynucleotide according to claim 2.

7. The polynucleotide of claim 4, which has a nucleotide sequence as set forth in SEQ ID NO: 4, and conservative variations thereof.

8. The polynucleotide of claim 1, wherein the SMRT co-repressor is a mouse SMRT α isoform.

9. The polynucleotide of claim 6, having an amino acid sequence as set forth in SEQ ID NO: 7 or conservative variations thereof.

10. The polynucleotide of claim 4, which has a nucleotide sequence as set forth in SEQ ID NO: 6.

11. The polynucleotide of claim 1, wherein the SMRT co-repressor is a mouse SMRT β isoform.

12. The polynucleotide of claim 11, having an amino acid sequence as set forth in SEQ ID NO: 9 or conservative variations thereof.

13. The polynucleotide of claim 11, which has a nucleotide sequence as set forth in SEQ ID NO: 8.

SUB
A23
CON't.

SUB
A24

SUB
A25

Sub C3

[illegible]

19. The polynucleotide of claim 1, which is operably linked to a second nucleotide sequence.

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C5

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claim 1.

~~gonucleot
e polynu
NO: 11 or
acids 103~~

Item 23, wherein

amino acids 497 to 523 of SEQ ID NO: 9.

25. The oligonucleotide of claim ~~23~~, which can hybridize specifically to a polynucleotide encoding SEQ ID NO: 5 or SEQ ID NO: 7, but not to a polynucleotide encoding SEQ ID NO: 9.

32. A complex, comprising a SMRT co-repressor of claim 26 and a member of the nuclear receptor superfamily (nuclear receptor).

33. The complex of claim 32, wherein the nuclear receptor is in the form of a dimer.

34. A method for identifying an agent that modulates the repressor potential of a SMRT co-repressor, the method comprising:

- 5 a) contacting a host cell with an agent,
 wherein the host cell contains a first expressible nucleotide
sequence operably linked to a first DNA regulatory element, and
 expresses a fusion polypeptide comprising a SMRT co-
repressor of claim 26, and a DNA binding domain of a first transcription
factor, which can specifically bind the first DNA regulatory element,
 and wherein binding of the DNA binding domain of the first
10 transcription factor to the first DNA regulatory element results in expression
of the first expressible nucleotide sequence; and
 b) detecting a change in the level of expression of the first
expressible nucleotide sequence due to contacting the host cell with the agent,
thereby identifying an agent that modulates the repressor potential of a SMRT
15 co-repressor.

35. A method for identifying an agent that modulates a function of a SMRT co-repressor, the method comprising:

- 20 a) contacting a SMRT co-repressor of claim 26,
a member of the nuclear receptor superfamily (nuclear
receptor), and
 an agent; and
 b) detecting an altered activity of the SMRT co-repressor in
the presence of the agent as compared to the absence of the agent, thereby
25 identifying an agent that modulates a function of the SMRT co-repressor.

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- a) contacting the molecule with the SMRT co-repressor of claim 26; and
- b) detecting specific binding of the molecule to the SMRT co-repressor, thereby identifying a molecule that interacts specifically with a SMRT co-repressor.

add c⁶⁰